

**UNIVERSITY OF MEDICINE AND PHARMACY TG.MURES
SCHOOL OF DOCTORAL STUDIES**

Personal contributions to anti-VEGF treatment of retinal diseases

PhD Thesis

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ABSTRACT

Retinal pathology is considered to be among the leading causes of vision loss in the elderly.

Thus, neovascular form of age-related macular degeneration, macular edema in diabetic retinopathy and branch or central retinal vein obstruction are injuries affecting the central portion of the retina (macula), which in a normal eye is responsible for central vision, details accuracy, allowing reading of small letters, driving and recognition of human facial features. Due to the presence of these retinal diseases, there is a severe deterioration of central vision and marked alterations in personal as well as in social quality of life of the affected person.

This paper is structured in two parts: the first part is theoretical and the second part consists of practical, personal research.

In the theoretical part, are reported findings from the literature on the phenomenon of angiogenesis, degenerative and vascular retinal eye diseases, respectively methods of diagnosis and treatment of these pathologies.

The personal research includes four clinical studies.

All four studies are involving the same type of treatment, respectively intravitreal administration of bevacizumab (Avastin, Genentech) in patients diagnosed with neovascular form of age-related macular degeneration, macular edema in diabetic retinopathy, macular edema in branch or central retinal vein obstruction.

The clinical trial was a prospective interventional type, whose purpose was to evaluate the effect of this treatment on the progression of mentioned above disease, respectively the ability to stop the disease, by comparing the recorded preoperative parameters with postoperative values at 1 year after the intervention.

This study aimed to follow the individual development of visual acuity (VA) parameter on intravitreal bevacizumab-treated patients, in representative lots, statistically adapted on random losses subjects and to record the evolution of VA correlated with central retinal thickness parameter (CRT). In

addition we proposed the observation of general characteristics of the patients included in our study group (age, sex, affected eye).

Materials and methods. The study consisted of 164 patients (172 eyes) diagnosed with age-related macular degeneration, 81 patients (94 eyes) with diabetic macular edema, 46 patients (46 eyes) with macular edema secondary to central retinal vein occlusion and 27 patients (28 eyes) diagnosed with macular edema secondary to branch retinal vein obstruction, treated at the Ophthalmology Clinic Tg. Mures. Enrolling of the cases in the trial has been successive, respecting the inclusion and exclusion criteria, the proposed postoperative observation period being 1 year.

Methods of study. Patients included in the study underwent a comprehensive preoperative eye exam: visual acuity assessment, slit lamp examination of the anterior and posterior pole, intraocular pressure measurement, optical coherence tomography examination and fluorescein angiography investigation. The followed parameters were: best corrected visual acuity and central retinal thickness. Preoperative examinations were repeated at 1, 3, 6 and 12 months postoperatively, the data being transversely collected.

Treatment protocol consisted of 2.5 mg / 0.1 mL intravitreal bevacizumab every four weeks, in triplicate (filling phase or loading dose) for each eye included in the study. Increasing the number of injections compared to standard protocol was performed on cases who presented clinical and functional improvement after three months of treatment, followed by relapses at intervals varying from a minimum of 3 months and maximum 12 months (losing 5 ETDRS letters or 1 ETDRS line, presence of intraretinian fluid, 100 microns increased central retinal thickness).

Results. The highest mean average visual acuity has been recorded at the first control, decreasing subsequently at the end of the follow-up period. At 12 months control, most significantly percentage of patients, who gained more than 3 ETDRS lines, was noticed in central retinal vein occlusion lot.

Percentage of patients with avoidance of moderate vision loss was highest in cases diagnosed with branch retinal vein occlusion. Moderate decrease of visual acuity was observed in diabetic macular edema.

Conclusions. There is a clear tendency of increasing VA parameter within a month initially, with a stabilization of its ranges between 3/6/12 months. Central retinal thickness has a decreasing value throughout the follow-up period of our study, its growth being explained by recurrent exudation phenomena. We didn't encountered major local or general complications, only minor sporadic side effects. We ascertain the efficiency of intravitreal bevacizumab in the short and medium term treatment.

Keywords: neovascular form of age-related macular degeneration, diabetic macular edema, central retinal vein occlusion, branch retinal vein occlusion, bevacizumab, visual acuity, central retinal thickness